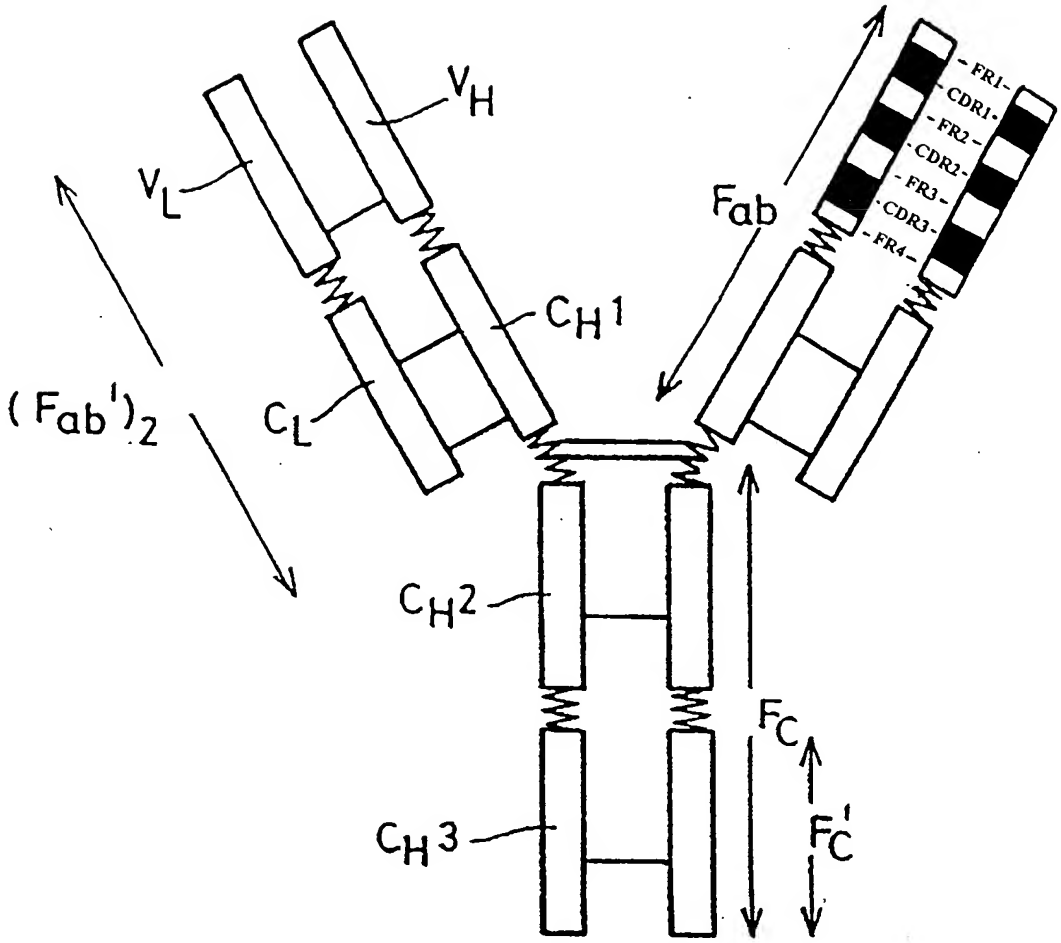
FIGURE 1



▭	domains
∧∧	inter-domain sections
——	disulphide bonds
V	variable
C	constant
L	light chain
H	heavy chain

FIGURE 2

A.

SEQ ID NO:59 - AME 33 light chain variable region amino acid sequence

EIVLTQSPGTLSLSPGERATLSCRASSSVPYIHWYQQKPGQAPRLLIYATSALASGI
PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQWLSNPPTFGQGTKLEIK

B.

SEQ ID NO:60 - AME 33 light chain variable region nucleic acid sequence

GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAG
AGCCACCCTCTCCTGCAGGGCCAGCTCAAGTGTACCGTACATCCACTGGTAC
CAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGCCACATCCGCTCT
GGCTTCTGGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTC
ACTCTCACCATCAGCAGACTGGAGCCTGAAGATTTTGCAGTGTATTACTGTCA
GCAGTGGCTGAGTAACCCACCCACTTTTGGCCAGGGGACCAAGCTGGAGATC
AAA

FIGURE 3

A.

SEQ ID NO:61 - AME 33 heavy chain variable region amino acid sequence

EVQLVQSGAEVKKPGESLKISCKGSGRTFTSYNMHWVRQMPGKGLEWMGAIYP
LTGDTSYNQKSKLQVTISADKSISTAYLQWSSLKASDTAMYYCARSTYVGGDW
QFDVWGKGTTVTVSS

B.

SEQ ID NO:62 - AME 33 heavy chain variable region nucleic acid sequence

GAGGTGCAGCTGGTGCAGTCTGGAGCAGAGGTGAAAAAGCCCGGGGAGTCT
CTGAAGATCTCCTGTAAGGGTTCTGGCCGTACATTTACCAGTTACAATATGCA
CTGGGTGCGCCAGATGCCCGGGAAAGGCCTGGAGTGGATGGGGGCTATTTAT
CCCTTGACGGGTGATACTTCCTACAATCAGAAGTCGAAACTCCAGGTCACCA
TCTCAGCCGACAAGTCCATCAGCACCGCCTACCTGCAGTGGAGCAGCCTGAA
GGCCTCGGACACCGCCATGTATTACTGTGCGAGATCGACTTACGTGGGCGGT
GACTGGCAGTTCGATGTCTGGGGCAAGGGGACCACGGTCACCGTCTCCTCA

FIGURE 4

A. Amino acid sequence of a human light chain framework region VkIII (A27) (DPK22) with interspersed CDR sequences labeled

(FRL1 - SEQ ID NO:71) CDRL1 (FRL2 - SEQ ID NO:72) CDRL2

EIVLTQSPGTLSLSPGERATLSCXXXXXXXXXX WYQQKPGQAPRLLIYXXXXXXX

(FRL3 - SEQ ID NO:73) CDRL3 (FRL4 - SEQ ID NO:74)

GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCXXXXXXXXX FGQGTKLEIK

B. Nucleic acid sequence of a human light chain framework region VkIII (A27) (DPK22) with interspersed CDR sequences labeled

(FRL1 - SEQ ID NO:75)

GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAG

CDRL1

CCACCCTCTCCTGCXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXTGGTACCAG

(FRL2 - SEQ ID NO:76) CDRL2

CAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATXXXXXXXXXXXXXXXXXXX

XXXGGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTC

(FRL3 - SEQ ID NO:77)

ACCATCAGCAGACTGGAGCCTGAAGATTTTGCAGTGTATTACTGTXXXXXXXXX

CDRL3 (FRL4 - SEQ ID NO:78)

XXXXXXXXXXXXXXXXXXXTTTGGCCAGGGGACCAAGCTGGAGATCAAA

FIGURE 5

A. Amino acid sequence of a human heavy chain framework region VH5-51 (DP-73) with interspersed CDR sequences labeled

(FRH1 - SEQ ID NO:79) CDRH1 (FRH2 - SEQ ID NO:80)
EVQLVQSGAEVKKPGESLKISCKGSXXXXXXXXXXWVRQMPGKGLEWMG

CDRH2 (FRH3 - SEQ ID NO:81)
XXXXXXXXXXXXXXXXXXQVTISADKSISTAYLQWSSLKASDTAMYYCAR

CDRH3 (FRH4 - SEQ ID NO:82)
XXXXXXXXXXXXWGKGTTVTVSS

B. Nucleic acid sequence of a human heavy chain framework region VH5-51 (DP-73) with interspersed CDR sequences labeled

(FRH1 - SEQ ID NO:83)
GAGGTGCAGCTGGTGCAGTCTGGAGCAGAGGTGAAAAAGCCCGGGGAGTCTCTG

CDRH1
AAGATCTCCTGTAAGGGTTCTXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

(FRH2- SEQ ID NO:84)
TGGGTGCGCCAGATGCCCGGGAAAGGCCTGGAGTGGATGGGG

CDRH2
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

CAGGTCACCATCTCAGCCGACAAGTCCATCAGCACCGCCTACCTGCAGTGGAGC

(FRH3 - SEQ ID NO:85)
AGCCTGAAGGCCTCGGACACCGCCATGTATTACTGTGCGAGAXXXXXXXXXXX

CDRH3 (FRH4 - SEQ ID NO:86)
XXXXXXXXXXXXXXXXXXXXXXXXXTGGGGCAAGGGGACCACGGTCACCGTCT

CCTCA

FIGURE 6

A.

SEQ ID NO:63 - AME 5 light chain variable region amino acid sequence

DIQMTQSPSSLSASVGDRVTITCRASSSVHYIHWYQQKPGKVPKLLIYATSGLAS
GVPSRFSGSGSGTDFTLTISSLQPEDVATYYCQTWTFNPPTFGGGTKVEIK

B.

SEQ ID NO:64 - AME 5 light chain variable region nucleic acid sequence

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGA
GACAGAGTCACCATCACTTGCAGGGCCAGCTCAAGTGTACATTACATC
CACTGGTACCAGCAGAAACCAGGGAAAGTTCCTAAGCTCTTGATCTAT
GCCACATCCGGCCTGGCTTCTGGGGTCCCATCTCGGTTCAGTGGCAGT
GGATCTGGGACAGATTTCACTCTCACCATCAGCAGCCTGCAGCCTGAA
GATGTTGCCACTTATTACTGCCAGACTTGGACTTTTAACCCTCCCACG
TTCGGCGGAGGGACCAAGGTGGAGATCAAA

FIGURE 7

A.

SEQ ID NO:65 - AME 5 heavy chain variable region amino acid sequence

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQGLEWMGAIY
PGNGDTSYNQKFKWRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARSTYYGGD
WQFDEWGKGTTVTVSS

B.

SEQ ID NO:66 - AME 5 heavy chain variable region nucleic acid sequence

CAGGTGCAGCTGGTGCAGTCTGGTGCTGAAGTGAAGAAGCCTGGGGCC
TCAGTGAAGGTGTCCTGCAAGGCATCTGGATACACCTTCACCAGCTAC
AATATGCACTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATG
GGAGCCATCTATCCTGGAAATGGTGATACAAGCTACAATCAGAAGTTT
AAATGGAGAGTCACCATGACCAGGGACACGTCCACGAGCACAGTCTAC
ATGGAGCTGAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGT
GCGAGATCGACTTATTACGGCGGTGACTGGCAGTTCGACGAGTGGGGC
AAAGGGACCACGGTCACCGTCTCCTCA

FIGURE 8

A. Amino acid sequence of a human light chain framework region VkI (DPK4) (A20) with interspersed CDR sequences labeled

(FRL1 - SEQ ID NO:87) (CDRL1) (FRL2 - SEQ ID NO:88) (CDRL2)
DIQMTQSPSSLSASVGDRVTITCXXXXXXXXXXXWYQQKPGKVPKLLIYXXXXXXX

(FRL3 - SEQ ID NO:89) (CDRL3) (FRL4 - SEQ ID NO:90)
GVPSRFSGSGSGTDFTLTISSLQPEDVATYYCXXXXXXXXXXFGGGTKVEIK

B. Nucleic acid sequence of a human light chain framework region VkI (DPK4) (A20) with interspersed CDR sequences labeled

(FRL1 - SEQ ID NO:91)
GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAG

(CDRL1)
TCACCATCACTTGCXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXTGGTACCAG

(FRL2 - SEQ ID NO:92) (CDRL2)
CAGAAACCAGGGAAAGTTCCTAAGCTCTTGATCTATXXXXXXXXXXXXXXXXXX

(CDRL2 cont.) (FRL3 - SEQ ID NO:93)
XXXXGGGGTCCCATCTCGGTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCT

CACCATCAGCAGCCTGCAGCCTGAAGATGTTGCCACTTATTACTGCXXXXXXXXX

(CDRL3) (FRL4 - SEQ ID NO:94)
XXXXXXXXXXXXXXXXXXXXTTCGGCGGAGGGACCAAGGTGGAGA

TCAAA

FIGURE 9

A. Amino acid sequence of a human heavy chain framework region VHI DP7/21-2 with interspersed CDR sequences labeled

(FRH1 - SEQ ID NO:95) (CDRH1) (FRH2 - SEQ ID NO:96)
QVQLVQSGAEVKKPGASVKVSCKAS<u>XXXXXXXXXXX</u>WVRQAPGQGLEWMG

(CDRH2) (FRH3 - SEQ ID NO:97)
<u>XXXXXXXXXXXXXXXXXX</u>RVTMTRDTSTSTVYMELSSLRSEDTAVYYCAR

(CDRH3) (FRH4 - SEQ ID NO:98)
<u>XXXXXXXXXXXX</u>WGKGTTVTVSS

B. Nucleic acid sequence of a human heavy chain framework region VHI DP7/21-2 with interspersed CDR sequences labeled

(FRH1 - SEQ ID NO:99)
CAGGTGCAGCTGGTGCAGTCTGGTGCTGAAGTGAAGAAGCCTGGGGCCTCAGTG

(CDRH1)
AAGGTGTCCTGCAAGGCATCT<u>XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX</u>TG

(FRH2 - SEQ ID NO:100) (CDRH2)
GGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGA<u>XXXXXXXXXXXXXX</u>

(CDRH2 cont.)
<u>XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX</u>AGAGTCACCATGAC

(FRH3 - SEQ ID NO:101)
CAGGGACACGTCCACGAGCACAGTCTACATGGAGCTGAGCAGCCTGAGATCTGA

(CDRH3)
GGACACGGCCGTGTATTACTGTGCGAGA<u>XXXXXXXXXXXXXXXXXXXXXXXXXX</u>

(CDRH3) (FRH4 - SEQ ID NO:102)
<u>XXXXXXXXXXX</u>TGGGGCAAAGGGACCACGGTCACCGTCTCCTCA

FIGURE 10

A.

SEQ ID NO:67 - AME 33 complete light chain amino acid sequence

EIVLTQSPGTLSLSPGERATLSCRASSSVPYIHWYQQKPGQAPRLLIYATSALASGIPDR
FSGSGSGTDFTLTISRLEPEDFAVYYCQQWLSNPPTFGQGTKLEIKRTVAAPSVFIFPPS
DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSST
LTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

- Constant Region is underlined

B.

SEQ ID NO:68 - AME 33 complete light chain nucleic acid sequence

GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAG
CCACCCTCTCCTGCAGGGCCAGCTCAAGTGTACCGTACATCCACTGGTACCAGCA
GAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGCCACATCCGCTCTGGCTTCTG
GCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCAT
CAGCAGACTGGAGCCTGAAGATTTTGCAGTGTATTACTGTCAGCAGTGGCTGAGT
AACCCACCCACTTTTGGCCAGGGGACCAAGCTGGAGATCAAACGAACTGTGGCTG
CACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCC
TCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGA
AGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAGGA
CAGCAAGGACAGCACCTACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGCAGA
CTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCG
CCCGTCACAAAGAGCTTCAACAGGGGAGAGTGTTAG

FIGURE 11

A. SEQ ID NO:69 - AME 33 complete heavy chain amino acid sequence

EVQLVQSGAEVKKPGESLKISCKGSGRTFTSYNMHWVRQMPGKGLEWMGAIYPLTG
DTSYNQKSKLQVTISADKSISTAYLQWSSLKASDTAMYYCARSTYVGGDWQFDVWG
KGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV**D**GV
EVHNAKT**K**PREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKA
KGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPV
LDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

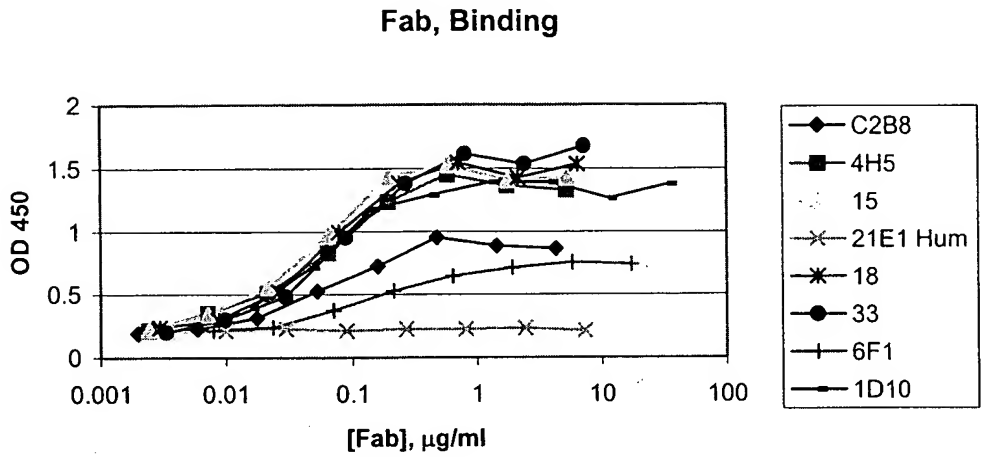
- Constant Region is underlined; the "D" at position 280 and "K" at position 290 are in bold

B. SEQ ID NO:70 - AME 33 complete heavy chain nucleic acid sequence

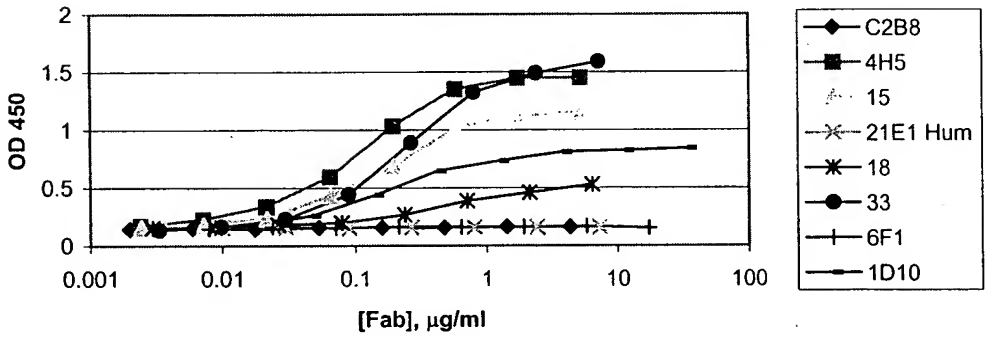
GAGGTGCAGCTGGTGCAGTCTGGAGCAGAGGTGAAAAAGCCCGGGGAGTCTCTG
AAGATCTCCTGTAAGGGTTCTGGCCGTACATTTACCAGTTACAATATGCACTGGGT
GCGCCAGATGCCCGGGAAAGGCCTGGAGTGGATGGGGGCTATTTATCCCTTGACG
GGTGATACTTCCTACAATCAGAAGTCGAAACTCCAGGTCACCATCTCAGCCGACA
AGTCCATCAGCACCGCCTACCTGCAGTGGAGCAGCCTGAAGGCCTCGGACACCGC
CATGTATTACTGTGCGAGATCGACTTACGTGGGCGGTGACTGGCAGTTCGATGTCT
GGGGCAAGGGGACCACGGTCACCGTCTCCTCAGCCTCCACCAAGGGCCCATCGGT
CTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCT
GCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGC
CCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACT
CCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACAT
CTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAGGTTGAGCC
CAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTG
GGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTC
CCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAG
GTCAAGTTCAACTGGTACGTG**GAC**GGCGTGGAGGTGCATAATGCCAAGACAAAG
CCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCC
TGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAG
CCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGA
ACCACAGGTGTACACCCTGCCCCCATCCCGGGACGAGCTGACCAAGAACCAGGTC
AGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGG
AGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTC
CGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG
CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACA
CGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATGA

FIGURE 12

A.



B.



C.

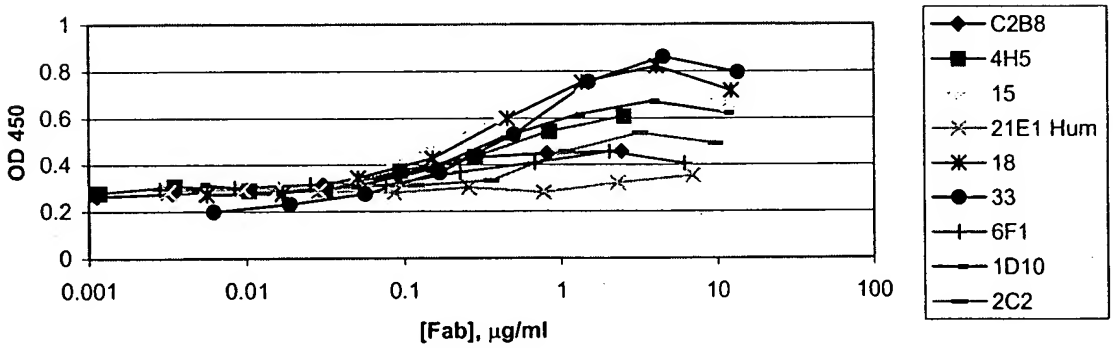
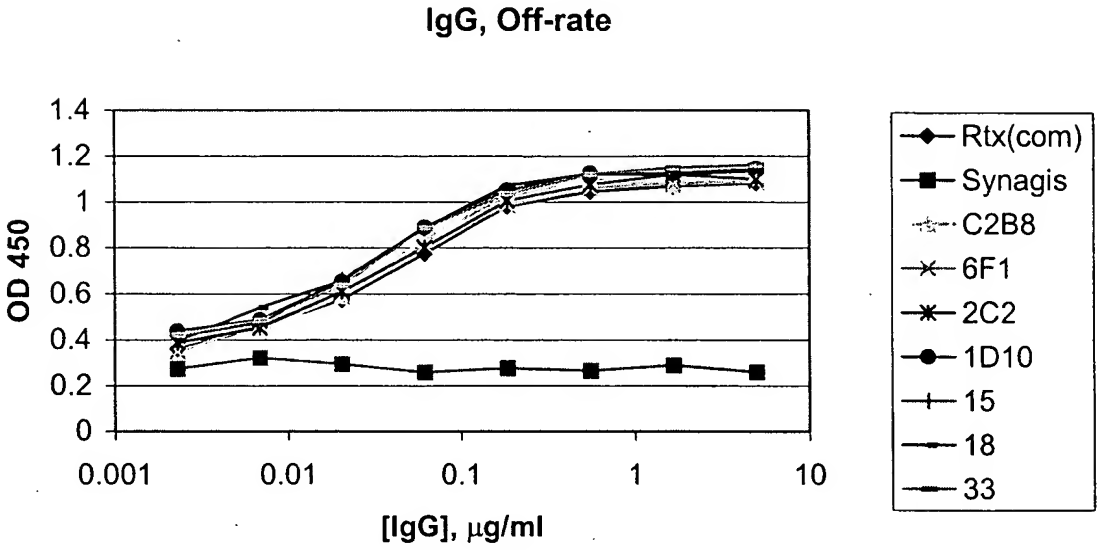


FIGURE 13

A.


IgG, Off-rate
OD 450
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0.001
0.01
0.1
1
10
[IgG], μg/ml
Rtx(com)
Synagis
C2B8
6F1
2C2
1D10
15
18
33

B.

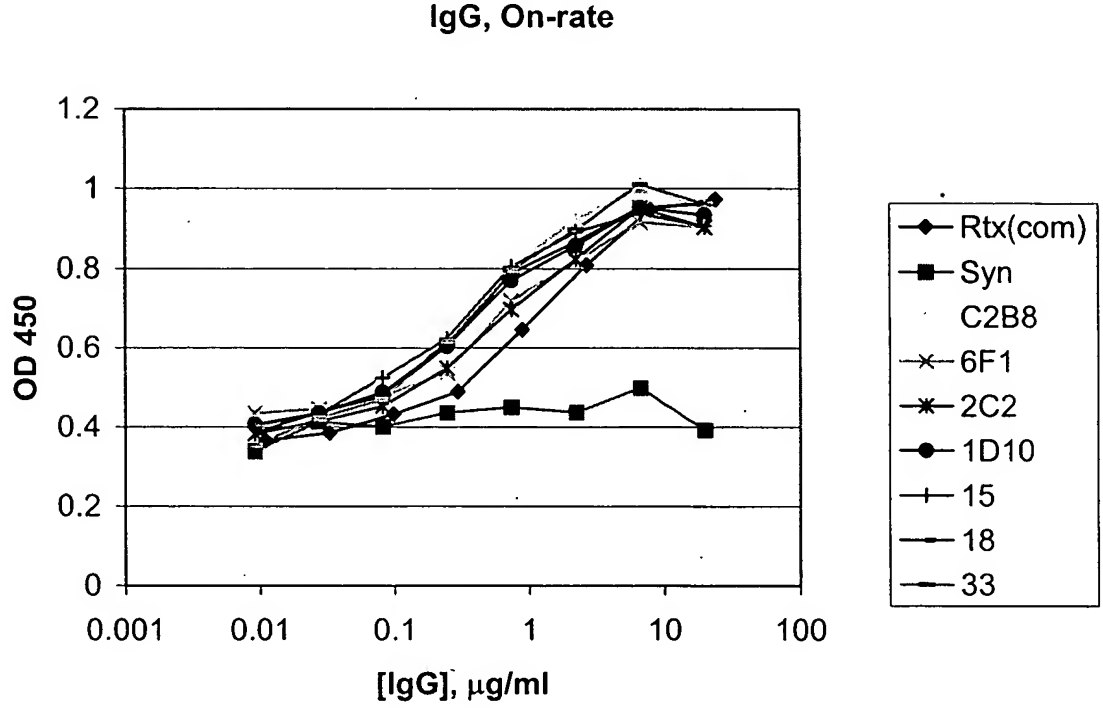
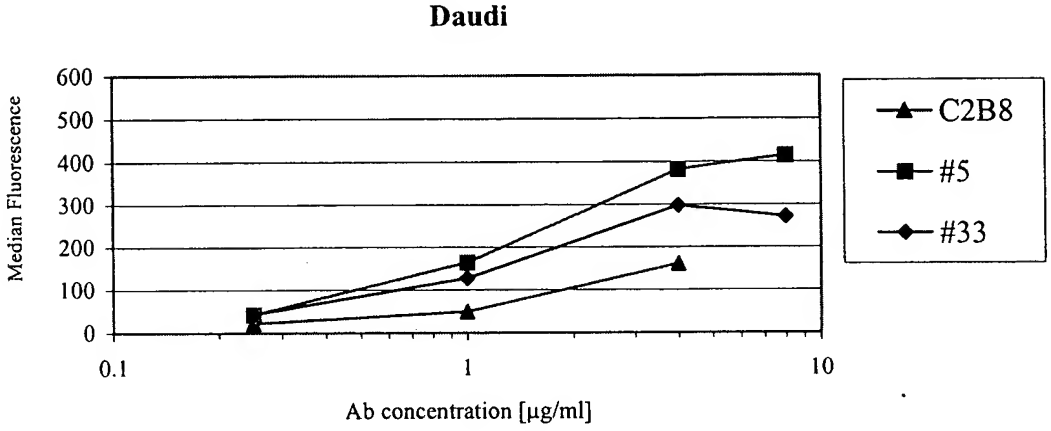
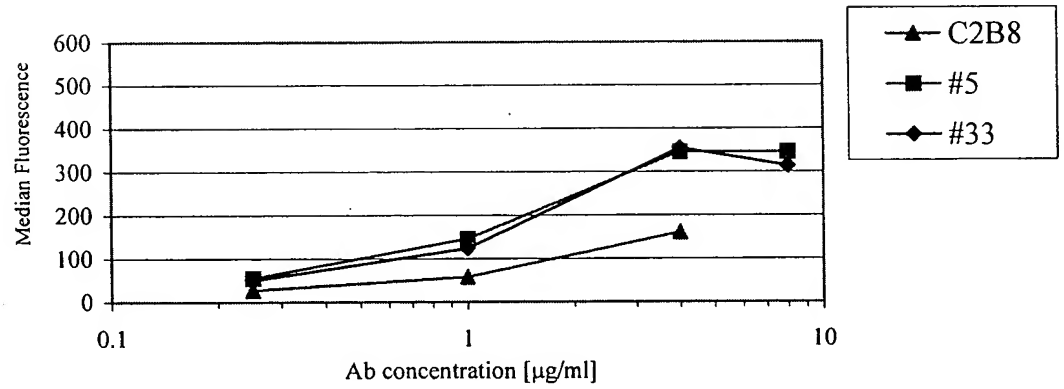

IgG, On-rate
OD 450
1.2
1
0.8
0.6
0.4
0.2
0
0.001
0.01
0.1
1
10
100
[IgG], μg/ml
Rtx(com)
Syn
C2B8
6F1
2C2
1D10
15
18
33

FIGURE 14

A.



B.



C.

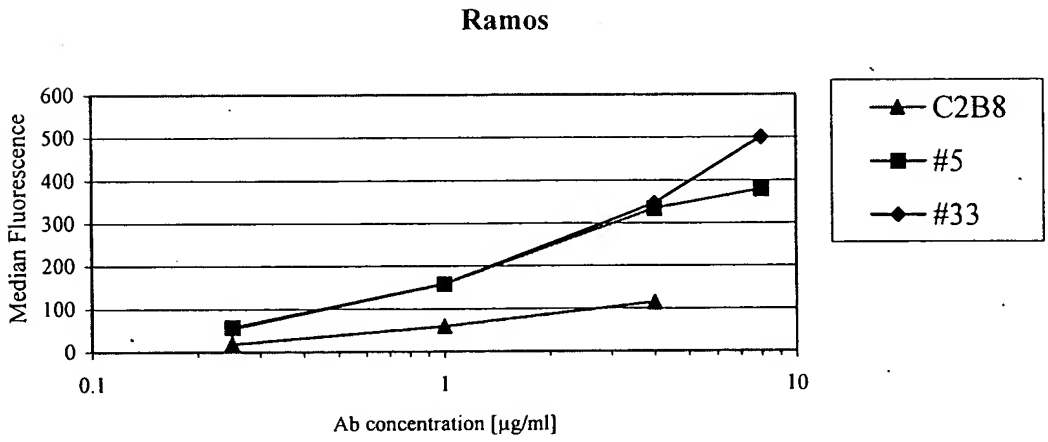


FIGURE 15

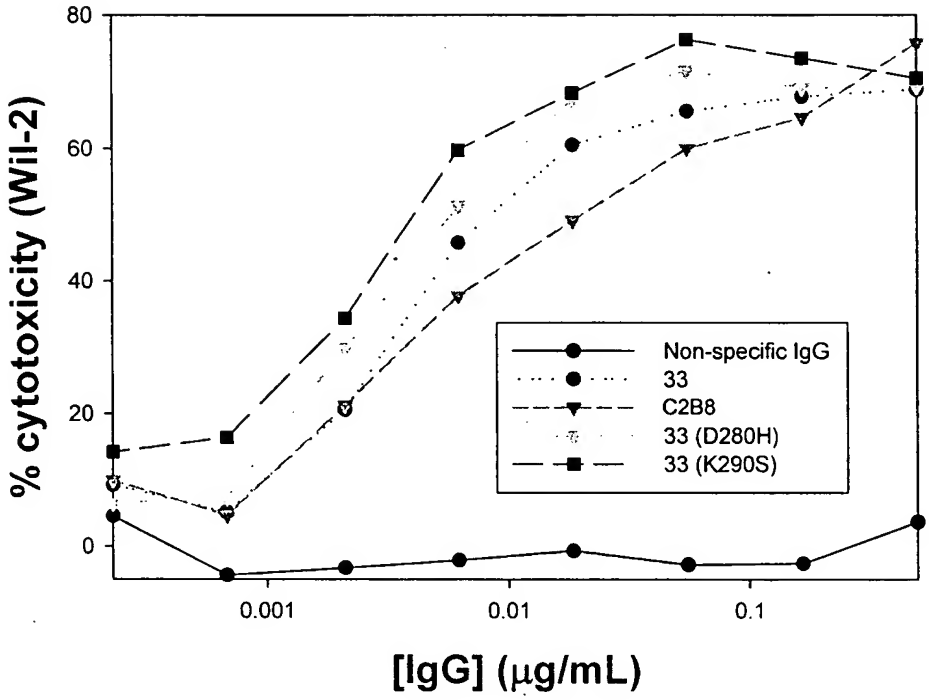
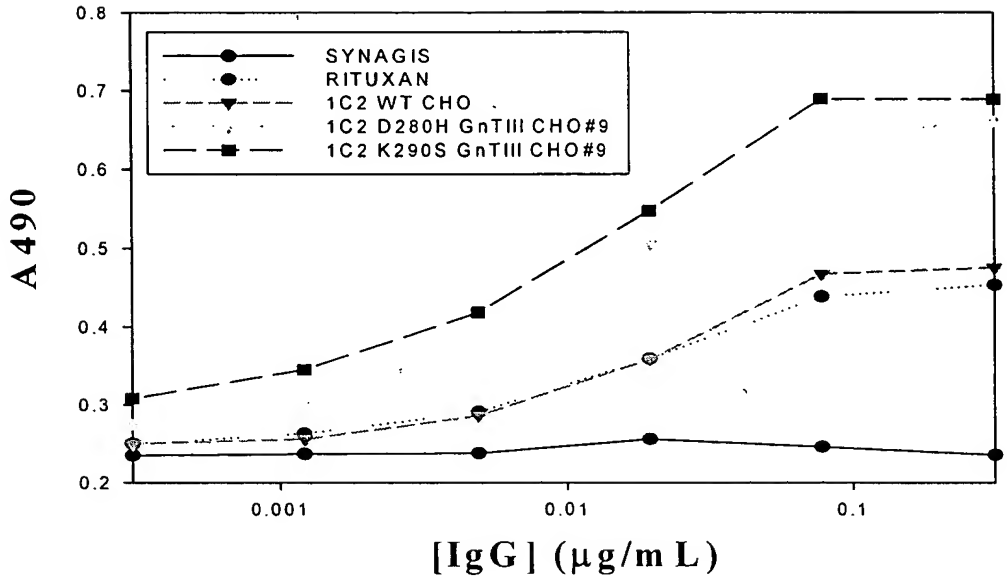

80
60
40
20
0
% cytotoxicity (Wil-2)
0.001
0.01
0.1
[IgG] (μg/mL)
Non-specific IgG
33
C2B8
33 (D280H)
33 (K290S)

FIGURE 16


SYNAGIS
RITUXAN
1C2 WT CHO
1C2 D280H GnTIII CHO#9
1C2 K290S GnTIII CHO#9
A490
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.001
0.01
0.1
[IgG] (µg/mL)

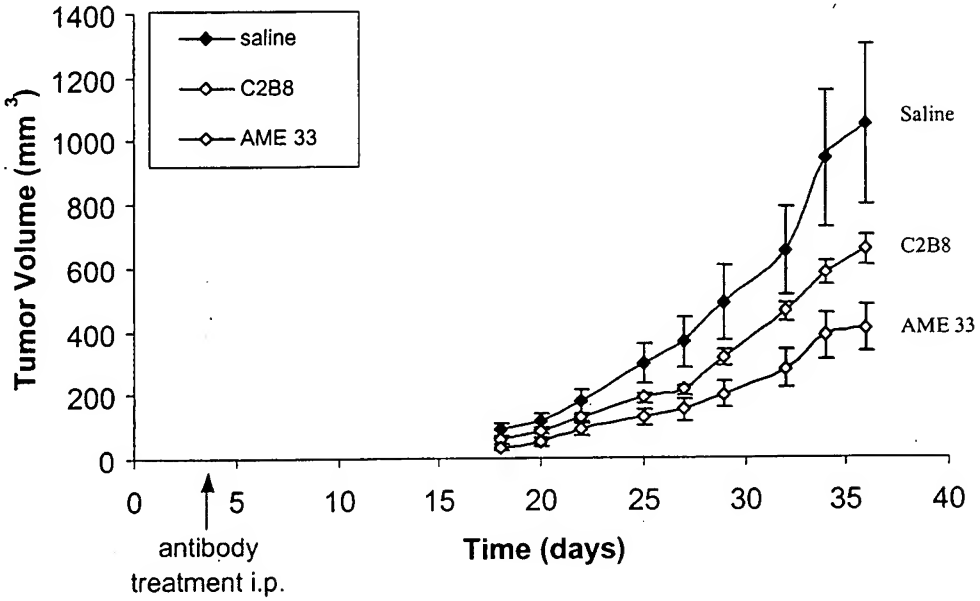

saline
C2B8
AME 33
Tumor Volume (mm 3)
1400
1200
1000
800
600
400
200
0
0
5
10
15
20
25
30
35
40
antibody
treatment i.p.
Time (days)
Saline
C2B8
AME 33

FIGURE 17